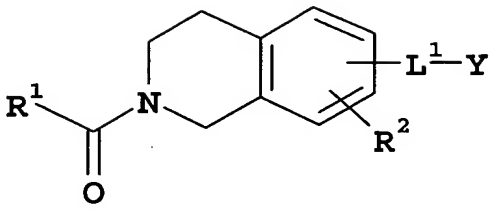
CLAIMS

What is claimed is:

1. A compound of formula (I):-



(I)

wherein:-

R^1 represents optionally substituted aryl, optionally substituted heteroaryl, $R^3NH\text{-}Ar^1\text{-}L^2$- or R^3-NH-C(=O)-NH-Ar^2-L^2-;

R^2 represents hydrogen, halogen, C_{1-4}alkyl or C_{1-4}alkoxy;

R^3 represents optionally substituted aryl or optionally substituted heteroaryl;

R^4 is alkyl, aryl, cycloalkyl, heteroaryl or heterocycloalkyl, or alkyl substituted by aryl, an acidic functional group, cycloalkyl, heteroaryl, heterocycloalkyl, $-S(O)_mR^5$, $-C(=O)-NY^3Y^4$ or $-NY^3Y^4$;

R^5 represents alkyl, alkenyl, alkynyl, aryl, arylalkyl, arylalkenyl, arylalkynyl, cycloalkyl, cycloalkylalkyl, cycloalkylalkenyl, cycloalkylalkynyl, cycloalkenyl, cycloalkenylalkyl, heteroaryl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, heterocycloalkyl or heterocycloalkylalkyl;

R^6 is hydrogen, alkyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl or heterocycloalkylalkyl;

R^7 is hydrogen, R^5 or alkyl substituted with alkoxy, cycloalkyl, hydroxy, mercapto, alkylthio or $-NY^3Y^4$;

R^8 is hydrogen or C_{1-4}alkyl;

R^9 and R^{11} are each independently selected from hydrogen or a group consisting of amino acid side chains, an acidic functional group, R^5, $-C(=O)-R^5$, or $-C(=O)-NY^3Y^4$, or alkyl substituted by an acidic functional group or by R^5, $-NY^3Y^4$, $-NH-C(=O)-R^5$, $-C(=O)-R^{12}-NH_2$, $-C(=O)-Ar^2-NH_2$, $-C(=O)-R^{12}-CO_2H$, or $-C(=O)-NY^3Y^4$;

or R^7 and R^9 together with the atoms to which they attached form a 3- to 6-membered heterocycloalkyl ring;

R^{10} represents C_{1-6}alkylene, optionally substituted by R^4;

R^{12} is an alkylene chain, an alkenylene chain, or an alkynylene chain;

R^{13} is alkyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl or heterocycloalkylalkyl;

Ar^1 represents a saturated, partially saturated or fully unsaturated 8- to 10-membered bicyclic ring system containing at least one heteroatom selected from O, S or N, optionally substituted by one or more aryl group substituents;

Ar^2 represents aryldiyl or heteroaryldiyl;

L^1 represents

(i) an alkenylene, alkylene or alkynylene linkage each optionally substituted by (a) carboxy, hydroxy, mercapto, cyano, oxo, $-S(O)_mR^4$, R^5, $-C(=O)-R^5$, $-C(=O)-OR^5$, $-N(R^6)-C(=O)-R^4$, $-N(R^6)-C(=O)-OR^4$, $-N(R^6)-SO_2-R^4$, $-NY^3Y^4$ or $-[C(=O)-N(R^7)-C(R^8)(R^9)]_p-C(=O)-NY^3Y^4$; or by (b) alkyl substituted by carboxy, hydroxy, mercapto, imidazolyl, $S(O)_mR^4$, $-C(=O)-NY^3Y^4$ or $-NY^3Y^4$;

(ii) a $-[C(=O)-N(R^7)-C(R^8)(R^9)]_p-$ linkage;

(iii) a $-Z^1-R^{10}-$ linkage;

(iv) a $-R^{10}-Z^1-R^{10}-$ linkage;

(v) a $-C(R^8)(R^{11})-[C(=O)-N(R^7)-C(R^8)(R^9)]_p-$ linkage; or

(vi) a $-L^3-L^4-L^5-$ linkage;

L^2 represents an alkylene chain;

L^3 and L^5 each independently represent a direct bond or an alkylene chain;

L^4 represents a cycloalkylene or heterocycloalkylene linkage;

Y^1 and Y^2 are independently hydrogen, alkenyl, alkyl, aryl, arylalkyl, cycloalkyl, heteroaryl or heteroarylalkyl; or the group $-NY^1Y^2$ may form a cyclic amine;

Y^3 and Y^4 are independently hydrogen, alkenyl, alkyl, alkynyl, aryl, cycloalkenyl, cycloalkyl, heteroaryl, heterocycloalkyl, or alkyl substituted by alkoxy, aryl, cyano, cycloalkyl, heteroaryl, heterocycloalkyl, hydroxy, oxo, $-NY^1Y^2$, or one or more $-CO_2R^6$ or $-C(=O)-NY^1Y^2$ groups; or the group $-NY^3Y^4$ may form a 5- to 7-membered cyclic amine which (i) may be optionally substituted

with one or more substituents selected from the group consisting of alkoxy, carboxamido, carboxy, hydroxy, oxo (or a 5-, 6- or 7-membered cyclic acetal derivative thereof) and R^7; (ii) may also contain a further heteroatom selected from O, S, SO_2, or NY^5; and (iii) may also be fused to additional aryl, heteroaryl, heterocycloalkyl or cycloalkyl rings to form a bicyclic or tricyclic ring system;

Y^5 is hydrogen, alkyl, aryl, arylalkyl, $-C(=O)-R^{13}$, $-C(=O)-OR^{13}$ or $-SO_2R^{13}$;

Z^1 is O, $S(O)_n$, NR^8, SO_2NR^8, $C(=O)NR^8$ or C(=O);

Y is carboxy or an acid bioisostere;

m is an integer 1 or 2;

n is zero or an integer 1 or 2; and

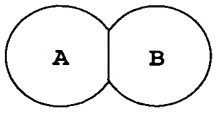
p is zero or an integer 1 to 4;

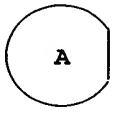
but excluding compounds where an oxygen, nitrogen or sulfur atom is attached directly to a carbon carbon multiple bond of an alkenylene or alkynylene residue;

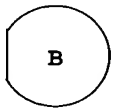
and the corresponding N-oxides and ester prodrugs thereof, and the pharmaceutically acceptable salts and solvates of such compounds, and the N-oxides and ester prodrugs thereof.

2. A compound according to claim 1 in which R^1 represents a group R^3-NH-Ar^1-L^2- in which:

L^2 is a straight or branched C_{1-6}alkylene chain;

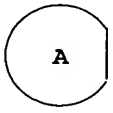
Ar^1 is an 8- to 10-membered bicyclic system 

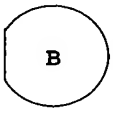
in which (i) ring 

is a 5- or 6-membered optionally substituted heterocycle, (ii) ring 

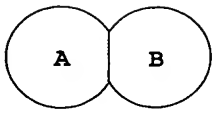
is a 5- or 6-membered optionally substituted heterocycle or an optionally substituted benzene ring, and (iii) the two rings are joined together by a carbon-carbon linkage or a carbon-nitrogen linkage; and

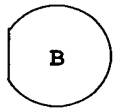
R^3 is an optionally substituted aryl.

3. A compound according to claim 2 in which 

is a 5-membered optionally substituted heterocycle, ring 

is an optionally substituted benzene ring, and the two rings are joined together by a carbon-carbon linkage.

4. A compound according to claim 2 in which  is an optionally substituted benzoxazolyl or an optionally substituted benzimidazolyl, each in which the benzene ring contains the optional substituents.

5. A compound according to claim 2 in which ring  is a benzene ring optionally substituted by one of C_{1-4} alkyl, C_{1-4} alkoxy, amino, halogen, hydroxy, C_{1-4} alkylthio, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, nitro or trifluoromethyl.

6. A compound according to claim 2 in which R^3 represents a 2-substituted phenyl.

7. A compound according to claim 6 in which R^3 represents 2-methylphenyl.

8. A compound according to claim 1 in which R^1 represents a group R^3-NH-C(=O)-NH-Ar^2-L^2- in which:

L^2 is a straight or branched C_{1-6}alkylene chain;

Ar^2 is an optionally substituted phenylene or an optionally substituted heteroaryldiyl; and

R^3 is an optionally substituted aryl group or an optionally substituted heteroaryl group.

9. A compound according to claim 8 in which Ar^2 is an optionally substituted m- or p-phenylene.

10. A compound according to claim 9 is which Ar^2 is a 3-substituted p-phenylene in which the substituent is ortho to the R^3-NH-C(=O)-NH- group.

11. A compound according to claim 8 in which Ar^2 is an optionally substituted azaheteroaryldiyl.

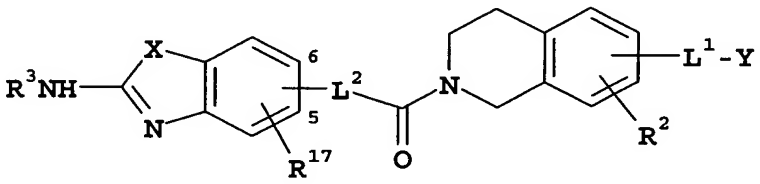
12. A compound according to claim 11 in which Ar^2 is pyridine-2,5-diyl, in which the R^3-NH-C(=O)-NH- group is adjacent to the pyridyl nitrogen atom, and which is substituted in the 4- or 6-position with a methyl or methoxy group.

13. A compound according to claim 8 in which R^3 is 2- or 3-methyl(or methoxy)phenyl.

14. A compound according to claim 8 in which R^3 is an optionally substituted pyridyl.

15. A compound according to claim 14 in which R^3 is 3-methyl-2-pyridyl.

16. A compound according to claim 1 of formula (Ia):-



(Ia)

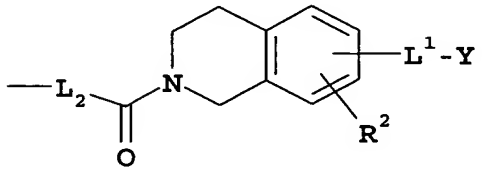
in which R^2, R^3, L^1, L^2 and Y are as defined in claim 1, X is O or NR^{18}, where R^{18} is hydrogen or C_{1-4}alkyl, and R^{17} is hydrogen or an aryl group substituent, and the corresponding N-oxides and ester prodrugs thereof, and the pharmaceutically acceptable salts and solvates of such compounds, and the N-oxides and ester prodrugs thereof.

17. A compound according to claim 16 in which R^3 represents an optionally substituted aryl.

18. A compound according to claim 16 in which R^{17} represents hydrogen, halo, C_{1-4} alkyl, or C_{1-4}alkoxy.

19. A compound according to claim 16 in which L^2 represents a straight or branched C_{1-6}alkylene chain.

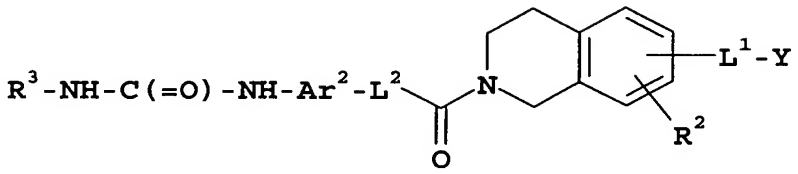
20. A compound according to claim 16 in which the group



is attached at the ring 6 position or at the ring 5 or 6 position when X is NR^{18} and R^{18} is C_{1-4}alkyl.

21. A compound according to claim 16 in which the group $—L^1-Y$ is attached at position 6 or 7 of the tetrahydroisoquinoline ring.

22. A compound according to claim 1 of formula (Ib):



(Ib)

in which R^2, R^3, Ar^2, L^1, L^2 and Y are as defined in claim 1, and the corresponding N-oxides and ester prodrugs thereof, and the pharmaceutically acceptable salts and solvates of such compounds, and the N-oxides and ester prodrugs thereof.

23. A compound according to claim 22 in which R^3 represents an optionally substituted aryl group or an optionally substituted heteroaryl group.

24. A compound according to claim 23 in which R^3 represents 2-methylphenyl or 3-methyl-2-pyridyl.

25. A compound according to claim 22 in which Ar^2 represents an optionally substituted phenylene or optionally substituted heteroaryldiyl.

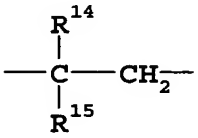
26. A compound according to claim 25 in which Ar^2 is p-phenylene or p-phenylene substituted in the 3-position by halo, C_{1-4}alkyl, C_{1-4}alkoxy, C_{1-4}alkylthio, C_{1-4}alkylsulfinyl or C_{1-4}alkylsulfonyl.

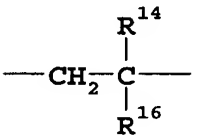
27. A compound according to claim 25 in which Ar^2 is pyridine-2,5-diyl, in which the R^3-NH-C(=O)-NH- group is adjacent to the pyridyl nitrogen atom, and which is substituted in the 4- or 6-position with a methyl or methoxy group.

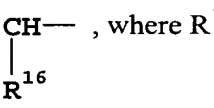
28. A compound according to claim 22 in which L^2 represents a straight or branched C_{1-6}alkylene chain.

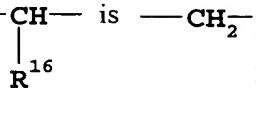
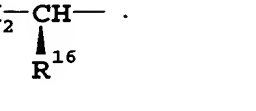
29. A compound according to claim 1 in which L^1 represents a C_{1-4}alkylene linkage optionally substituted by C_{1-4}alkyl, aryl, heteroaryl, $-N(R^6)-C(=O)-R^4$, $-N(R^6)-C(=O)-OR^4$, $-N(R^6)-SO_2-R^4$, $-NY^3Y^4$ or $-[C(=O)-N(R^7)-C(R^8)(R^9)]_p-C(=O)-NY^3Y^4$, or alkyl substituted by carboxy, hydroxy, mercapto, imidazolyl, $-C(=O)-NY^3Y^4$ or $-NY^3Y^4$.

30. A compound according to claim 29 in which the C_{1-4}alkylene linkage is an ethylene linkage.

31. A compound according to claim 30 in which L^1 represents a group  , where R^{14} is hydrogen or C_{1-4}alkyl and R^{15} represents hydrogen or C_{1-4}alkyl; or where R^{14} is hydrogen and R^{15} represents aryl, heteroaryl, $-N(R^6)-C(=O)-R^4$, $-N(R^6)-C(=O)-OR^4$, $-N(R^6)-SO_2-R^4$, $-NY^3Y^4$ or $-[C(=O)-N(R^7)-C(R^8)(R^9)]_p-C(=O)-NY^3Y^4$, or alkyl substituted by carboxy, hydroxy, mercapto, imidazolyl, $-C(=O)-NY^3Y^4$ or $-NY^3Y^4$.

32. A compound according to claim 30 in which L^1 represents a group  , where R^{14} is hydrogen or C_{1-4}alkyl and R^{16} represents C_{1-4}alkyl; or where R^{14} is hydrogen and R^{16} represents aryl, heteroaryl, $-N(R^6)-C(=O)-R^4$, $-N(R^6)-C(=O)-OR^4$, $-N(R^6)-SO_2-R^4$, $-NY^3Y^4$ or $-[C(=O)-N(R^7)-C(R^8)(R^9)]_p-C(=O)-NY^3Y^4$, or alkyl substituted by carboxy, hydroxy, mercapto, imidazolyl, $-C(=O)-NY^3Y^4$ or $-NY^3Y^4$.

33. A compound according to claim 32 in which L^1 is a group  , where R^{16} represents $-N(R^6)-C(=O)-R^4$, or $-N(R^6)-SO_2-R^4$.

34. A compound according to claim 33 in which the group  is  .

35. A compound according to claim 1 selected from:
3-{((4-methyl-2-*o*-tolylamino-benzoxazol-6-yl)-acetyl)-1,2,3,4-tetrahydro-isoquinolin-6-yl}-butanoic acid;
3-{((2-*o*-tolylamino-benzoxazol-6-yl)-acetyl)-1,2,3,4-tetrahydro-isoquinolin-7-yl}-butanoic acid,;
3-phenyl-3-{((2-*o*-tolylamino-benzoxazol-6-yl)-acetyl)-1,2,3,4-tetrahydro-isoquinolin-6-yl}-propanoic acid;
3-cyclohexyl-3-{((2-*o*-tolylamino-benzoxazol-6-yl)-acetyl)-1,2,3,4-tetrahydro-isoquinolin-6-yl}-propanoic acid;
3-(pyrid-4-yl)-3-{((2-*o*-tolylamino-benzoxazol-6-yl)-acetyl)-1,2,3,4-tetrahydro-isoquinolin-7-yl}-propanoic acid;
3-{((2-*o*-tolylamino-benzoxazol-6-yl)-acetyl)-1,2,3,4-tetrahydro-isoquinolin-8-yl}-but-2-enoic acid;
3-{((2-*o*-tolylamino-benzoxazol-6-yl)-acetyl-1,2,3,4-tetrahydro-isoquinolin-8-yl}-butanoic acid;
3-{2-[(2-*o*-tolylamino-benzoxazol-6-yl)-carbonyl]-1,2,3,4-tetrahydro-isoquinolin-6-yl}-butanoic acid;
{5-(3-methoxy-4-[3-(2-methylphenyl)ureido]-phenylacetylamino)-1,2,3,4-tetrahydro-isoquinolin-8-yl}-butanoic acid;
2-(2,6-dichloro-benzoylamino)-3-[2-(2,6-dichloro-benzoyl]-1,2,3,4-tetrahydro-isoquinolin-7-yl]-propionic acid;
3-phenyl-3-{((2-*o*-tolylamino-benzoxazol-6-yl)-acetyl)-1,2,3,4-tetrahydro-isoquinolin-7-yl}-propanoic acid;
3-{(2-*o*-tolylamino-benzoxazol-6-yl)-acetyl)-1,2,3,4-tetrahydro-isoquinolin-6-yl}-butanoic acid;
3-(pyrid-4-yl)-3-{((2-*o*-tolylamino-benzoxazol-6-yl)-acetyl)-1,2,3,4-tetrahydro-isoquinolin-7-yl}-propanoic acid, enantiomer A;
3-(pyrid-4-yl)-3-{((2-*o*-tolylamino-benzoxazol-6-yl)-acetyl)-1,2,3,4-tetrahydro-isoquinolin-7-yl}-propanoic acid, enantiomer B;
and the corresponding N-oxides and ester prodrugs thereof, and the pharmaceutically acceptable salts and solvates of such compounds, and the N-oxides and ester prodrugs thereof.

36. A pharmaceutical composition comprising an effective amount of a compound according to claim 1 or a corresponding N-oxide or ester prodrug thereof, or a pharmaceutically acceptable salt or solvate of such a compound, or an N-oxide or ester prodrug thereof, in association with a pharmaceutically acceptable carrier or excipient.

37. A method for the treatment of a human or non-human animal patient suffering from, or subject to, a condition which can be ameliorated by the administration of an inhibitor of $\alpha 4\beta 1$ mediated cell

adhesion comprising administering to said patient an effective amount of a compound according to claim 1 or a corresponding N-oxide or ester prodrug thereof, or a pharmaceutically acceptable salt or solvate of such a compound, or an N-oxide or ester prodrug thereof.

38. A method for the treatment of a patient suffering from, or subject to, asthma comprising administering to said patient an effective amount of a compound according to claim 1 or a corresponding N-oxide or ester prodrug thereof, or a pharmaceutically acceptable salt or solvate of such a compound, or an N-oxide or ester prodrug thereof.

39. A method for the treatment of a patient suffering from, or subject to, an inflammatory disease comprising administering to said patient an effective amount of a compound according to claim 1 or a corresponding N-oxide or ester prodrug thereof, or a pharmaceutically acceptable salt or solvate of such a compound, or an N-oxide or ester prodrug thereof.

40. A method for the treatment of a human or non-human animal patient suffering from, or subject to, a condition which can be ameliorated by the administration of an inhibitor of $\alpha 4\beta 1$ mediated cell adhesion comprising administering to said patient an effective amount of a composition according to claim 36.

41. A method for the treatment of a patient suffering from, or subject to, asthma comprising administering to said patient an effective amount of a composition according to claim 36.

42. A method for the treatment of a patient suffering from, or subject to, an inflammatory disease comprising administering to said patient an effective amount of a composition according to claim 36.